Appendix 1

Which methods are used to confirm the diagnosis of acute promyelocytic leukemia?

P – Acute promyelocytic leukemia
I – Karyotyping, cytogenetics, flow cytometry, fluorescence in situ hybridization, reverse transcriptase polymerase chain reaction or morphology of bone marrow cells
O – Diagnosis

Acute promyelocytic leukemia AND (Differential diagnosis OR Flow cytometry OR karyotyping OR Cytogenetic Analysis OR Fluorescence in situ hybridization OR Polymerase chain reaction OR bone marrow examination OR electrophoresis OR monoclonal OR immunofixation OR light chain OR immunoglobulin OR symptoms OR anemia OR fractures OR bone lesions OR hypercalcemia OR renal failure OR renal insufficiency OR clinical chemistry tests OR cytodiagnosis OR hematologic tests OR immunologic tests) AND (Diagnosis/Narrow) = 89
1st selection: 27
2nd selection: 6

Which laboratory tests are used to evaluate coagulopathies in acute promyelocytic leukemia?

P – Acute promyelocytic leukemia
I – Coagulogram, D-Dimer, fibrinogen, platelets, prothrombin time, activated partial thromboplastin time, fibrin degradation products
O – Bleeding

Acute promyelocytic leukemia AND (blood coagulation disorders OR hemorrhage OR bleeding) AND (fibrinogen degradation products OR D-dimer OR fibrinogen OR blood platelets OR blood coagulation tests) = 143
1st selection: 5

How can the risk of relapse of patients with acute promyelocytic leukemia be stratified?

P – Acute promyelocytic leukemia
I – Risk stratification
O – Recurrence

Leukemia, Promyelocytic, Acute AND Risk AND (Treatment Failure OR Recurrence) = 123
1st selection: 4

How should coagulopathies in acute promyelocytic leukemia be treated?

P – Acute promyelocytic leukemia
I – Coagulopathy
O – Treatment

Acute promyelocytic leukemia AND (blood coagulation disorders) AND (Therapy/Broad[filter]) = 153
1st selection: 38
2nd selection: 11

Which anthracycline should be used in induction therapy for acute promyelocytic leukemia, in terms of response rate, overall survival and toxicity?

P – Acute promyelocytic leukemia
I – Anthracycline (daunorubicin, doxorubicin, idarubicin or mitoxantrone)
O - Response rate, overall survival and toxicity

Acute promyelocytic leukemia AND (Daunorubicin OR Doxorubicin OR Idarubicin OR Cytarabine OR Mitoxantrone) AND (Therapy/broad[filter] OR Comparative study OR Comparative studies OR Epidemiologic methods)) = 664
1st selection: 38
2nd selection: 8

Is induction with arsenic trioxide superior to induction with all-trans retinoic acid plus anthracycline?

P – Acute promyelocytic leukemia
I – Arsenic trioxide or arsenicals
C – All-trans retinoic acid

Acute promyelocytic leukemia AND (arsenic trioxide OR arsenicals) AND (tretinoin) AND (Therapy/Narrow) = 6
1st selection: 2

What are the risk factors for the development of differentiation syndrome?

P – Acute promyelocytic leukemia
I – Risk factors
O – Differentiation syndrome

Acute promyelocytic leukemia AND (tretinoin* OR ATRA OR ATRA-syndrome OR ATRA syndrome OR retinoic acid differentiation syndrome OR retinoic acid syndrome OR differentiation syndrome) AND risk =231
1st selection: 7

Is the prophylactic use of corticosteroids in patients with acute promyelocytic leukemia able to prevent Differentiation syndrome?

P – Acute promyelocytic leukemia/Differentiation syndrome
I – Corticosteroid, prophylaxis

C – All-trans retinoic acid
O – Prevent Differentiation syndrome

Acute promyelocytic leukemia AND steroids AND tretinoin =191
1st selection: 4

What is the best therapeutic conduct for Differentiation syndrome?

P – Differentiation syndrome
I – Corticosteroid, diuretics, interruption of ATRA
O – Improvement in symptoms

Acute promyelocytic leukemia AND tretinoin =2320
1st selection: 29

What is the best therapeutic conduct for pseudotumor cerebri syndrome?

P - Pseudotumor cerebri syndrome in patients with acute promyelocytic leukemia
I - Corticoid

Acute promyelocytic leukemia AND (pseudotumor cerebri) AND (Therapy/Broad) = 31
1st selection: 21

Is prophylaxis of the central nervous system indicated for a specific group of patients with acute promyelocytic leukemia?

P – Acute promyelocytic leukemia
I – Methotrexate or cytarabine
O – Prophylaxis of the central nervous system

Acute promyelocytic leukemia AND (methotrexato OR cytarabine) AND (meningitis OR central nervous system infections OR liquor OR infiltrating) = 2
1st selection: 2

Are there benefits with the use of cytarabine in acute promyelocytic leukemia?

P – Acute promyelocytic leukemia
I – Cytarabine
O – Complete remission, disease-free survival, overall survival

Acute promyelocytic leukemia AND (Cytarabine) AND (Therapy/broad[filter] OR Comparative study OR Comparative studies OR Epidemiologic methods)) = 401
1st selection: 9

What is the role of transplantation in relapse of acute promyelocytic leukemia and when should allogeneic and autologous transplants be indicated?

P – Acute promyelocytic leukemia
I – Allogeneic transplant
C – Autologous transplant
O – Complete remission, disease-free survival, overall survival

Acute promyelocytic leukemia AND (transplantation OR transplant) AND allogeneic AND autologous AND (Therapy/Broad) = 46
1st selection: 3

How to make the diagnosis of molecular relapse? Which method, quantitative or qualitative polymerase chain reaction, is most recommended?

P – Acute promyelocytic leukemia
I – Quantitative polymerase chain reaction,
C – Qualitative polymerase chain reaction
O – Molecular relapse

Acute promyelocytic leukemia AND (polymerase chain reaction) AND (quantitative OR qualitative) AND (recurrence OR remission) = 42
Acute promyelocytic leukemia AND Reverse Transcriptase Polymerase Chain Reaction AND (recurrence OR remission) =163
1st selection: 6

What are the best therapeutic options for hematologic and extramedullary relapse?

P – Relapse or recurrence and acute promyelocytic leukemia
I – All-trans retinoic acid or arsenic trioxide or systemic chemotherapy
O – Remission

Acute promyelocytic leukemia AND (recurrence OR remission) AND (Therapy/Narrow) = 56
1st selection: 5

How should the patient with acute promyelocytic leukemia during pregnancy be treated?

P – Pregnant women with acute promyelocytic leukemia
I – All-trans retinoic acid or cytarabine or anthracycline (daunorubicin or idarubicin)
O – Complete remission, disease-free survival, overall survival

Acute promyelocytic leukemia AND pregnancy AND (Therapy/Broad[filter]) = 58
1st selection: 26

How should an elderly patient with acute promyelocytic leukemia be treated?

P – Acute promyelocytic leukemia, elderly
I – All-trans retinoic acid or cytarabine or anthracycline (idarubicin or daunorubicin)
O – Complete remission, disease-free survival, overall survival

Acute promyelocytic leukemia AND age AND (tretinoin OR Cytarabine OR Idarubicin OR daunorubicin) = 719
1st selection: 5

How should minimal residual disease in acute promyelocytic leukemia be monitored?

P – Acute promyelocytic leukemia
I – Polymerase chain reaction
O – Minimal residual disease

Acute promyelocytic leukemia AND neoplasm residual = 272
1st selection: 7